IB. AMENDMENTS TO THE CLAIMS

Cancel claims 10, 15-21, and 24 without prejudice to renewal.

Please enter the amendments to claims 1-9 and 11, as shown below.

1. (Currently amended) A ~~pharmaceutically useful compound~~ pharmaceutical composition ~~for inhibiting immunostimulation by immunostimulatory sequence oligodeoxynucleotides (ISS-ODN), wherein the ISS-ODN contain a hexamer region consisting of at least one CpG nucleotide motif flanked by two 5' purines and two 3' pyrimidines (ISS-ODN), the composition~~ comprising:

(a) a nucleic acid molecule comprising ~~an oligonucleotide containing a hexamer region having the~~ a hexameric nucleotide sequence of the formula 5'-Purine-Purine-[Y]-[Z]-~~Pyrmidine~~ Pyrimidine-Pyrimidine-3' or 5'-Purine-Purine-[Y]-[Z]-~~Pyrmidine~~ poly(Pyrimidine)-3';

where Y is any naturally occurring or synthetic nucleotide except cytosine and Z is any naturally occurring or synthetic nucleotide [[;however,]] , wherein when Y is not guanosine or inosine, Z is guanosine or inosine; and

(b) a pharmaceutically acceptable carrier.

2. (Currently amended) The ~~compound~~ composition according to claim 1 where Y is guanosine or inosine.

3. (Currently amended) The ~~compound~~ composition according to claim 1 where Y is inosine and Z is inosine or guanosine.

4. (Currently amended) The ~~compound~~ composition according to claim 1 where Y is guanosine and Z is guanosine or an unmethylated cytosine.

5. (Currently amended) A ~~pharmaceutically useful compound~~ pharmaceutical composition ~~for inhibiting immunostimulation by immunostimulatory sequence oligodeoxynucleotides~~ comprising :

(a) a nucleic acid molecule comprising a hexameric ~~an oligonucleotide containing a hexamer region having a~~ nucleotide sequence ~~consisting of~~ AAGGTT; and

(b) a pharmaceutically acceptable carrier.

6. (Currently amended) A ~~pharmaceutically useful compound~~ pharmaceutical composition ~~for inhibiting immunostimulation by immunostimulatory sequence oligodeoxynucleotides~~ comprising :

(a) a nucleic acid molecule comprising a hexameric ~~an oligonucleotide containing a hexamer region having a~~ nucleotide sequence ~~consisting of~~ AAGCTT; and

(b) a pharmaceutically acceptable carrier.

7. (Currently amended) A ~~pharmaceutically useful compound~~ pharmaceutical composition ~~for inhibiting immunostimulation by immunostimulatory sequence oligodeoxynucleotides~~ comprising :

(a) a nucleic acid molecule comprising a hexameric ~~an oligonucleotide containing a hexamer region having a~~ nucleotide sequence ~~consisting of~~ AGGGCT; and

(b) a pharmaceutically acceptable carrier.

8. (Currently amended) A ~~pharmaceutically useful compound~~ pharmaceutical composition ~~for inhibiting immunostimulation by immunostimulatory sequence oligodeoxynucleotides~~ comprising :

(a) a nucleic acid molecule comprising a hexameric ~~an oligonucleotide containing a hexamer region having a~~ nucleotide sequence ~~consisting of~~ GAGGTT; and

(b) a pharmaceutically acceptable carrier.

9. (Currently amended) A ~~pharmaceutically useful compound~~ pharmaceutical composition ~~for inhibiting immunostimulation by immunostimulatory sequence oligodeoxynucleotides~~ comprising:

~~an oligonucleotide containing a hexamer region having a~~ (a) a nucleic acid molecule comprising a hexameric nucleotide sequence selected from the group ~~of sequences~~ consisting of AAGCTT, AGGCTC, GAGCTT, GGGCTT, AAGCTC, AGGCTC, GAGCTC, GGGCTC, AAGCCC, AGGCCC, GAGCCC, GGGCCC, AGGCCT, GAGCCT, GGGGCT, TTGCAA, AATGTT, GGGGTT, ~~and~~ AAGCCC , AAGGTT, AGGGCT, and GAGGTT; and

(b) a pharmaceutically acceptable carrier.

10. (Canceled)

11. (Currently amended) The ~~compound~~ composition according to any of Claims 1 through 9 wherein the ~~oligonucleotide compound~~ nucleic acid is conjugated to a peptide.

12. (Original) A kit for use in gene therapy or gene immunization consisting of any of the immunoinhibitory compounds of Claims 1 through 11 in a sterile vial and a recombinant expression vector in a sterile vial.

13. (Original) The kit according to Claim 12, wherein the immunoinhibitory compound and the recombinant expression vector are contained in the same sterile vial.

14. (Original) A method for inhibiting the immunostimulatory activity of ISS-ODN in contact with a population of vertebrate cells which includes lymphocytes or monocytes comprising contacting the population of vertebrate cells with an immunoinhibitory amount of an oligonucleotide containing a hexamer region having the nucleotide sequence 5'-Purine--Purine-[Y]-[Z]- Pyrmidine--Pyrimidine-3' or 5'-Purine--Purine-[Y]-[Z]-[[Pyrmidine-]] poly(Pyrimidine)-3', where Y is any naturally occurring or synthetic nucleotide except cytosine and Z is any naturally occurring or synthetic nucleotide ;however, when Y is not guanosine or inosine, Z is guanosine or inosine; wherein a reduction in Th1 type immune response measured in the population of vertebrate cells indicates that the desired inhibition of ISS-ODN immunostimulatory activity has been achieved.

15.-21. (Canceled)

22. (Original) A method for reducing inflammation in a host in response to a microbial infection of the host comprising administering an immunoinhibitory amount of an oligonucleotide containing a hexamer region having the nucleotide sequence 5'-Purine-Purine-[Y]-[Z]-Pyrmidine -Pyrimidine-3' or 5'-Purine-Purine-[Y]-[Z]-Pyrmidine poly(Pyrimidine)-3', where Y is any naturally occurring or synthetic nucleotide except cytosine and Z is any naturally occurring or synthetic nucleotide;however, when Y is not guanosine or inosine, Z is guanosine or inosine; wherein a reduction in Th1 type immune responses against the infectious microbe measured in the host or a reduction in other clinical signs of inflammation in the host indicates that the desired reduction in host inflammation has been achieved.

23. (Original) A method for modulating the immunostimulatory activity of an ISS-ODN in contact with a population of vertebrate cells which includes lymphocytes or monocytes comprising contacting the population of vertebrate cells with an immunoinhibitory amount of an oligonucleotide containing a hexamer region having the nucleotide sequence 5'-Purine--Purine-

[Y]-[Z]-Pyrmidine--Pyrimidine-3' or 5'-Purine--Purine-[Y]-[Z]-Pyrmidine poly(Pyrimidine)-3', wherein Y is any naturally occurring or synthetic nucleotide except cytosine and Z is any naturally occurring or synthetic nucleotide ;however, when Y is not guanosine or inosine, Z is guanosine or inosine; and wherein a reduction in Th1 type immune responses measured in the population of vertebrate cells indicates that the desired inhibition of ISS-ODN immunostimulatory activity has been achieved.

24. (Canceled)

25. (Original) A method for boosting a Th2 type immune response to an antigen comprising contacting a population of antigen stimulated vertebrate cells including lymphocytes with an immunostimulatory amount of an oligonucleotide containing a hexamer region having the:

5'-Purine--Purine-[Y]-[Z]-Pyrmidine--Pyrimidine-3' or 5'-Purine--Purine-[Y]-[Z]-Pyrmidine poly(Pyrimidine)-3', wherein Y is any naturally occurring or synthetic nucleotide except cytosine and Z is any naturally occurring or synthetic nucleotide ;however, when Y is not guanosine or inosine, Z is guanosine or inosine ; wherein a reduction in Th1 type immune responses or increase in antigen stimulated IgG1 production measured in the population of vertebrate cells indicates that the desired boost in Th2 type immune responses to the antigen has been achieved.

26. (Original) A method for identifying IIS-ODN which inhibit the immunostimulatory activity of ISS-ODN comprising:

(a) contacting a population of antigen stimulated immune cells with an ISS-ODN to induce lymphocyte proliferation in; IFNβ, IFN-α, IFN-γ, IL-12 and IL-18 cytokine secretion from; IgG1 antibody production by; or IgE suppression in, the population of antigen-stimulated immune cells;

(b) measuring any change the number of lymphocytes or levels of secreted cytokines and/or levels of IgE or IgG1 antibodies in the population of antigen-stimulated cells after contact with the ISS-ODN;

(c) contacting the population of antigen stimulated cells with a candidate IIS-ODN inhibitory oligonucleotide; and

(d) measuring any change in the number of lymphocytes or levels of secreted IFNβ, IFN-α, IFN-γ, IL-12 and IL-18 cytokines and/or levels of IgE or IgG1 antibodies in the population of antigen-stimulated cells after contact with the oligonucleotide, wherein a decline in any of the measured values for lymphocyte proliferation, cytokine secretion or IgG1 antibody production, as well as an increase in IgE antibody production, as compared

to the measurements taken in step (b) indicates that the oligonucleotide inhibits the immunostimulatory activity of the ISS-ODN of step (a).

27. (Original) The method according to Claim 26, wherein the candidate inhibitory oligonucleotide contains a hexamer region having the nucleotide sequence 5'-Purine--Purine-[Y]-[Z]-Pyrmidine--Pyrimidine-3' or 5'-Purine--Purine-[Y]-[Z]-Pyrmidine poly(Pyrimidine)-3', wherein Y is any naturally occurring or synthetic nucleotide except cytosine and Z is any naturally occurring or synthetic nucleotide; however, when Y is not guanosine or inosine, Z is guanosine or inosine.

28. (Original) A pharmaceutically useful compound comprising an oligonucleotide identified according to the method of Claim 26 as one which inhibits the immunostimulatory activity of ISS-ODN.

29. (Original) A method of detecting ISS-ODN immunostimulatory activity in a host comprising:

(a) obtaining a sample of immune cells from the host, which cells are believed to been exposed to an antigen or autoantigen;

(b) measuring the levels of lymphocyte proliferation in; IFNβ, IFN-α, IFN-γ, IL-12 and IL-18 cytokine secretion from; IgG1 antibody production by; or IgE suppression in, the sample of host immune cells;

(c) contacting the sample of host immune cells with an immunoinhibitory oligonucleotide (IIS-ODN); and,

(d) measuring any change in the number of lymphocytes or levels of secreted IFNβ, IFN-α, IFN-γ, IL-12 and IL-18 cytokines and/or levels of IgE, IgG2 or IgG1 antibodies in the sample of host immune cells after contact with the IIS-ODN, wherein a decline in any of the measured values for lymphocyte proliferation, cytokine secretion or IgG2 antibody production, as well as an increase in IgG1 or IgE antibody production, as compared to the measurements taken in step (b), indicates that the ISS-ODN subject to inhibition by the IIS-ON is present in the sample of host immune cells.